demonstrates that transformation of *Brassica* was within the level of skill in the art prior to the date that the application was filed. Hence the absence of a specific disclosure of a method for expressing monoclonal antibodies in *Brassica* should not be viewed as a lack of enablement because those skilled in the art would be able to transform *Brassica* using the teachings of the specification.

More generally, the Examiner's comments understate the state of the art. For example, Ma et al., *Nature Med.*, 4:601-606 (1998), cited by the Examiner, refers to expression of immunoglobulin molecules for passive immunization against tooth decay by transformed tobacco plants. A companion article in the same journal (Tacket et al., *Natiure Med.*, 4:607-609 (1998) reports production of a recombinant bacterial vaccine antigens in potato. As reported in the summary (submitted herewith) Tacket et al. were able to induce immunity to the bacterial antigens in humans by ingestion of the transformed potato. According to another authority, Kipriyanov et al., *Generation Of Monoclonal Antibodies*, Molecular Biology, 12:173 (1999) at 179 (also submitted herewith) "Plants are capable of synthesizing and assembling virtually every kind of antibody molecule, ranging from the smallest antigen-binding domains and fragments to full-length and even multimeric antibodies." In sum, the Examiner appears to have considered the level of skill in the art to be limited to Applicants' disclosure for transforming *Arabidopsis*, which it clearly is not. In view of the considerably broader level of skill in the art, as evidenced by documents submitted herewith, Applicants respectfully submit that the rejection of claims 5, 11 and 13-16 should be withdrawn.

Claims 3-5, 9-11 and 13-16 also stand rejected on the grounds that the scope of enablement is not commensurant with the scope of the claims sought. Specifically, the Examiner contends that claims that include immunoglobulins of the IgM isotype are not enabled by

examples of the production of chimeric monoclonal antibodies wherein the constant region is derived from IgG. According to the enclosed article, Kipriyannov et al, *Generation of Monoclonal Antibodies., supra* at 201, "the construction of chimeric and humanized antibodies offers the opportunity of tailoring the constant region to the requirements of the antibody." As examples, Kipriyanov et al. refer to selection of subtypes of the IgG isotype specific for cell mediated cytotoxicity.

Thus the current state of the art allows construction of immunologlobulin molecules of isotypes selected by the investigator. IgG and IgM, are specific examples of isotypes used to illustrate the scope of applicants' invention. Because the state of the art allows specific selection of isotypes and even sub isotypes, the rejection of claims 3-5, 9-11 and 13-16 for lack of enablement should be withdrawn.

Rejections For Indefiniteness

Claims 3 and 9 stand rejected as indefinite, as the Examiner contends it is not clear whether the claims refer to the monoclonal antibody or the chimeric antibody as an antecedent. Applicants respectfully traverse this rejection.

Both rejected claims have the same structure. In both rejected claims the preamble refers to "the step of preparing." The only occurrence of the verb "preparing" in the claims from which the rejected claims depend refers to "chimeric monoclonal antibodies" as the verb's object. Naturally occurring antibodies from which the chimeric antibodies are prepared are discussed only in elements a) and b) of the antecedent claim, while chimeric antibodies and the only use of the verb "preparing" is in element c) of the antecedent claim. Hence the claim language requires that the step of "preparing" refers to preparing a chimeric monoclonal antibody whose

complementarity determining regions are from a monoclonal antibody induced by immunization, and whose constant region is corresponds with that of the mammal to be treated.

Rejections For Lack Of Novelty

Claims 1, 6 and 7 stand rejected as anticipated under 35 U.S.C. § 102(b) by Lehner, United States patent 5,352,446. According to the Examiner, Lehner discloses the oral administration of murine monoclonal antibodies to *S. mutans* for the treatment and prevention of dental caries in man. Applicants respectfully traverse this rejection.

Each of applicants claims is limited to a chimeric monoclonal antibody to a cariogenic organism. As nothing in the cited reference refers to use of chimeric monoclonal antibodies for the treatment and prevention of dental caries, Lehner does not anticipate any of applicants' claims.

Rejections For Obviousness

Claims 1-4, 6-10, 12 and 17 stand rejected under 35 U.S.C. § 103(a). According to the Examiner, Ma et al. disclose the production of chimeric monclonal antibodies to *S. mutans* in tobacco plants. Further, the chimeric monoclonal antibodies of Ma et al. differ from applicants' in that the antibodies produced by Ma et al. are entirely of murine origin. The Examiner contends that it would have been obvious to prepare chimeric antibodies in which the light chains are murine while the heavy chains are human, to prepare humanized monoclonal antibodies with the specificity of those prepared by Ma et al. Applicants respectfully traverse this rejection.

The chimeric antibodies described in Ma et al. article were of the IgA isotype. The survival in the human oral cavity of chimeric antibodies were compared with antibodies of the IgG isotype of murine origin. Adair, United States patent 5,877,293 refers to a humanized mouse monoclonal antibody specific for carcinoembryonic antigen. As stated in the '293 patent, the purpose of humanization is simply to reduce the incidence of "HAMA" – human anti mouse reaction – not to engage the effector apparatus of the human immune response. Even if the cited references could be properly combined, which applicants do not believe is the case, no combination would teach or suggest applicants' claimed invention.

Applicants' invention includes a method for treatment of dental caries wherein a chimeric antibody is capable of both specifically recognizing cariogenic organisms, and eliciting an effector response *to such organisms from the host immune system.* Neither Ma et al. nor Adair, nor any combination of the references teach or suggest this capability.

Unless the constant region of a chimeric monoclonal antibody is capable of activating the host immune system, the binding of antigen to a target organism could at most provide a method for its detection or the delivery of a drug or toxin to the site recognized. No teaching of which applicants are aware suggests the use of chimeric antibodies to bring the effector apparatus of the human immune system to bear on an infectious or otherwise pathological site in the body.

As the cited references do not teach or suggest the claimed invention, the rejection for obviousness should be withdrawn.

The claims are to inventions made jointly by both inventors. For all times pertinent hereto, Dr. Anderson was employed by Washington Dental Service, an assignee of this application, while Dr. Shi was employed by the Regents of the University of California.

Applicants respectfully suggest that their claims are in condition for allowance, and request issuance of a notice thereof. The Assistant Commissioner is hereby authorized to charge any required fees to Deposit Account No. 131 241, for the pendency of this application and for all fees that may be charged to a deposit account, or to credit any overpayment thereto.

Respectfully submitted
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